

**Summary of Infectious Disease and Environmental Health Administration,
DHMH Center for TB Control and Prevention
TB Epidemiologic Studies Consortium (TBESC) Site Research Studies**

(October 2001 – September 2011)

Task Order 1 – Umbrella contract for TBESC site (CDC Contract no. 200-2001-0081):

Principal Investigator: Wendy Cronin, PhD (DHMH)
Co-Principal Investigator: Susan Dorman, MD (Hopkins School of Medicine)
Co-Principal Investigator: Jonathan Golub, PhD (Hopkins School of Medicine)
Project Manager: Andrea Palmer, MSc (UMBC)

The umbrella contract funds salaries (or partial salaries) for the above staff, as well as travel for TBESC staff to semi-annual TBESC meetings, as required per the contract. Task Order 1 also provides support funds as needed to complete the tasks below. Funds for project support must be pre-approved by the CDC Division of TB elimination.

Task Order 2 – “Prospective Evaluation of Patient Risks Factors and Behaviors, Immunogenetic Susceptibility, and Surrogate Markers for Tuberculosis Disease”

Site Principal Investigator: Susan Dorman, MD (Hopkins School of Medicine)
Study Coordinator: Elizabeth “Bee” Munk, RN, BSN (Hopkins School of Medicine)

Study Site: Baltimore City
(10 TBESC sites)

Current status: Data collection is complete for all sites and data are being cleaned and analyzed.

The objectives of this study were to (1) identify surrogate markers of the protective immune response of *M. tuberculosis*, and (2) identify genetic determinants of susceptibility to tuberculosis infection and disease. Little has been known about the immunologic and genetic factors that increase the risk for tuberculosis infection and progression to active disease. Baltimore City US-born culture-positive pulmonary tuberculosis cases and their close contacts were recruited for study enrollment. Blood drawn for immunologic testing was sent to the TB Research Unit at Case Western Reserve University (CWRU) and blood drawn for immunogenetic testing was sent to the Division of AIDS, STD, and TB Laboratory Research (DASTLR) at the Centers for Disease Control and Prevention (CDC). Dr. Cronin is leading a manuscript workgroup to evaluate HIV testing in contact investigations.

Task Order 8 – “An Analysis of Molecular Epidemiology of Multi-drug Resistant *M. tuberculosis* in the United States”

Site Principal Investigator: Wendy Cronin, PhD (DHMH)
Study Coordinator: Frances Maurer, RN, MSN (Hopkins School of Medicine)

Study Site: Statewide
(15 TBESC sites)

Current status: Data collection is complete for all sites and data are being cleaned and analyzed.

The purpose of this study was to develop a comprehensive national TB genotyping registry for TB case-patients with MDR-TB and to assess the molecular epidemiology of MDR-TB in the U.S. It was anticipated that this ongoing surveillance of MDR-TB cases through collection of genotyping data and epidemiologic investigations would help clarify the dynamics of MDR-TB transmission, factors contributing to spread, and identification and evaluation of potential areas for appropriate interventions. Epidemiologic and genotyping data was be collected through a standardized interview from all multi-drug resistant *M. tuberculosis* (MDR-TB) case-patients, and from selected non-MDR-TB patients who have the same *M. tuberculosis* strain.

Task Order 9 – “Enhanced Surveillance to Identify Missed Opportunities for Prevention of Tuberculosis in the Foreign-Born”

Site Principal Investigator: Wendy Cronin, PhD (DHMH)
Study Coordinator: Frances Maurer, RN, MSN (Hopkins School of Medicine)

Study Site: State of Maryland (random sampling)
(22 TBESC sites)

Current status: Data collection is complete for all sites and data are being cleaned and analyzed.

The purpose of this study was to improve tuberculosis control efforts among the foreign-born, who now account for more than half of all tuberculosis cases diagnosed in the United States and Canada. Randomly selected foreign-born tuberculosis patients were interviewed using a standardized tool. Maryland was very active on the protocol team for this study. Ms. Maurer achieved an over 75% acceptance rate for the study as of Jan 30, 2006, and won the interviewer prize, while Prince George’s County won the local health department study support award. Dr. Cronin is leading a writing group to evaluate the impact of required overseas medical examinations on TB disease diagnosed among refugees and immigrants after arrival in the US.

Task Order 13 – “Study of factors associated with acceptance of, adherence to, and toxicity from treatment for latent tuberculosis infection”

Site Principal Investigator: Wendy Cronin, PhD (DHMH)
Prior Project Coordinators for Phases 1 and 2: TK Dorjee, RN, Cara Endyke-Doran, RN, MSN, MPH
Current Project Coordinator, Phase 3: Susanna Collins, MSc (Hopkins School of Medicine)

Project Site: Baltimore City and Wicomico – expanded to Statewide
(13 TBESC sites)

Current status: Data collection is complete for all sites and data are being cleaned and analyzed.

The purpose of this study was to better understand the scope of treatment of latent tuberculosis infection (LTBI) in the United States and Canada and to elucidate factors associated with acceptance and completion of treatment. The underlying premise of this study was that a complex interplay of cultural, social, economic, structural, clinical, and interpersonal factors influences rates of acceptance and completion of treatment. Phase 1 identified clinics that treat patients with LTBI.

Phase 2 required record review to determine factors associated with starting and completing treatment for LTBI. Phase 3 required interviews with LTBI candidates to identify potentially modifiable factors associated with acceptance and completion of, and possibly toxicity from, treatment of LTBI. Candidates for treatment of LTBI were interviewed when offered treatment; those participants who accepted treatment were interviewed before, during, and after treatment.

Task Order 18 – Evaluation of new blood tests in the diagnosis of latent tuberculosis infection in health care workers

Study Principal Investigator: Susan Dorman, MD (Hopkins School of Medicine)
Project Coordinator: Elizabeth “Bee” Munk, RN, BSN (Hopkins School of Medicine)
Research Nurse: Kathryn Taylor, RB, BSN (Hopkins School of Medicine)

Project Site: Baltimore City – Johns Hopkins Healthcare Workers
(4 TBESC sites)

Current status: Data collection is complete for all sites and data are being cleaned and analyzed.

The purpose of this project was to evaluate three tests for latent TB infection in healthcare workers. One test was the routinely used PPD tuberculin skin test. The other two tests were blood tests that measure immune response to TB antigens (interferon gamma release assays, or IGRAs). The purpose of this project was to understand the long-term reproducibility of these blood test results (over time in one person), the most appropriate test to identify latent TB infection, the frequency of reversion, and the cost-effectiveness, feasibility, and acceptability of using these tests. Participants included healthcare workers who are routinely tested for TB infection. Participants who agreed to be in the study received the three tests and were interviewed every 6 months over a period of 18 months. Dr. Dorman is leading the main analysis and manuscript writing for this study

Task Order 23 – National study of determinants of early diagnosis, prevention, and treatment of TB in the African-American community

Site Principal Investigator: Jonathan Golub, PhD (Hopkins School of Medicine)
Project Coordinator (MD): Frances Maurer, RN, MSN contract: (Hopkins School of Medicine)
Project Coordinator (VA): Suzanne Keller, MPH (Virginia Dept of Health)

Project Site: Statewide, Washington, DC, and selected Virginia Counties
(8 TBESC sites)

Current status: Data collection is complete for all sites and data are being cleaned and analyzed.

The purpose of this project was to quantify delays in TB diagnosis in African Americans, specifically related to infectious disease surveillance and response; infectious disease elimination; behavioral, social and economic research in infectious diseases; and special populations and infectious diseases. The data acquired through this study greatly aids the TBESC research priority area, specifically helping to develop, evaluate and implement strategies to reduce and eliminate health disparities associated with TB disease. Participants included US-born African American TB cases and US-born white controls. Participants who agreed to be in the study were interviewed. Clinic records, including contact investigation

records, were also reviewed to determine missed opportunities for diagnosis of their TB disease.

Task Order 25 – Tuberculosis mortality in the United States: epidemiology and prevention opportunities

Site Principal Investigator: Jonathan Golub, PhD (Hopkins School of Medicine)
Project Coordinator (MD): Gina Maltas, RN, BSN (Hopkins School of Medicine)

Project Site: Statewide
(10 TBESC sites)

Current status: Data collection is complete for all sites and data are being cleaned and analyzed.

The purpose of this study was to evaluate and describe mortality among a cohort of patients diagnosed with TB, assess the prevalence of TB-related deaths, identify risk factors for TB-related deaths, and determine the proportion of TB-related deaths that were preventable. Data sources included public and private medical records and death certificates. Participants for this study included TB patients who were reported in 2005 and 2006 and who died before or during treatment; controls were TB patients reported in 2005 and 2006 who did not die during treatment. Information generated by this study will result in improved understanding of the causes of TB-related deaths, and will create the evidence-basis for public health interventions aimed at reducing TB deaths in the US.

Task Order 26 – Integration of *Mycobacterium tuberculosis* genotyping into routine TB program practice: testing and refinement of a method to prioritize clusters for investigation

Study Principal Investigator: Wendy Cronin, PhD, MT (ASCP) (DHMH)
Project Coordinator: Susanna Collins, MSc (Hopkins School of Medicine)

Project Site: Statewide
(4 TBESC sites)

Current status: Data collection is completed for all sites and data are being cleaned and analyzed.

The purpose of this project was to develop a real-time surveillance algorithm using routinely collected information (TB genotyping and public health surveillance data), to identify and prioritize genotypic clusters representing potential TB transmission events. An evidence-based algorithm was developed that prioritizes genotype clusters for local investigation and possible public health action (e.g., TB outbreaks). In addition, the direct resources required for local cluster investigations and use of a location-based tool to improve contact investigations were evaluated. Finally, the public health impact of project cluster investigations was measured (e.g., new contacts identified, screened, and treated for latent TB infection, new TB cases diagnosed, evaluation of completeness of contact investigations). Participants included culture-positive TB patients whose isolates have matching genotypes (genotypic cluster). Study results will help local programs more efficiently use genotyping data available for all culture positive TB patients in the United States.

Task Order 27 – Determining the programmatic costs and benefits of using a nucleic acid amplification (NAA) assay for TB diagnosis within the United States

Site Principal Investigator: Susan E. Dorman, MD (Hopkins School of Medicine)
Project Manager: Gina Maltas, RN, BSN (Hopkins School of Medicine)
Project Coordinator: Sandy Chon, MHS (Hopkins School of Medicine)

Project Site: Baltimore City and Baltimore, Prince George's, Montgomery Counties
(4 TBESC sites)

Current status: Data collection is complete in the Maryland TBESC site and data are being cleaned.

The purpose of this study was to measure the costs and benefits of using the "MTD," "NAA," or a comparable nucleic acid amplification assay in various programmatic settings for AFB smear-positive pulmonary TB suspects: either congregate settings (i.e., nursing homes, homeless shelters, school dormitories, and hospitals) or other settings where populations (i.e., HIV-infected persons, foreign born persons) likely to have atypical mycobacterial infection resulting in false-positive AFB smears complicate the evaluation of TB disease. In addition, the study measured costs and benefits of this test in persons who are likely to have false-negative AFB smears (i.e., HIV-infected or other immuno-suppressed persons) and who are at risk of transmitting TB and/or dying without treatment prior to receipt of culture results. Medical records were reviewed for known and suspected TB patients who have had an NAA tests performed on sputum and other specimens. Hospital costs for various procedures to diagnose and treat TB were collected and reviewed.